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Letters to the Editor

Sir,

Pindolol in the treatment of complicated myocardial infarction

In a letter to the Editor, Baber and Lewis[1] question the suggestion made in our study[2] that oral prophylactic treatment with beta-adrenoceptor blocking drugs should not start too early after the infarction. They point to the results of the Hansteen study[3] with propranolol, performed in high-risk patients comparable to those in the pindolol study and mention other studies where the reduction in mortality was higher in patients who entered the study 5–9 days ('early') after the infarction than in those who entered the study later.

The results of the pindolol study, however, suggest that the treated patients who entered the study up to 5 days after the infarction fared worse than those who were admitted later. To our knowledge, in none of the studies with a statistically significant reduction in total mortality was treatment begun earlier than 5 days after the infarction.

There is obviously confusion about the use of the term 'early', because in the pindolol paper it refers to the time up to the fifth day after the infarction while Baber and Lewis in their letter call 'early' the time from the fifth day onwards.

In addition, Lewis stated in a previous paper[4] that the difference between pooled 'early' (up to 48 h) and late entry studies showed for the early entry studies 'a small positive effect, but this had no statistical or clinical significance' contrary to the 'highly significant effect of beta-blockade on total mortality' in the pooled analysis of seven late-entry trials.

Our data shows a similar tendency and are therefore well in accordance with Dr Lewis' previous analysis.

We agree, however, with the suggestion that patient groups with different benefit from the treatment may have been entered at different time points in different studies.

The possibility that the time of entry may not be the only decisive factor for the outcome of the study has been discussed in our paper on p. 374.

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[3] Hansteen V, Moinichen E, Lorentsen E, *et al.* One year's treatment with propranolol after myocardial infarction: Preliminary report of Norwegian multicentre trial. Br Med J 1982; 284: 155–60.
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Sir,

Pindolol in the treatment of complicated myocardial infarction

In a letter to the Editor, Dr Prescott[1] criticizes our using a discriminant analysis allowing for the exclusion of main effects while keeping interactions with these main effects in the model. Moreover, he states that 'an occasional significant finding should not cause great surprise'. On pages 368 and 369 of our paper[2] ('Statistical analysis'), we have stated explicitly that this discriminant analysis was executed in the exploratory sense only — as well as all other analyses reported except the analysis of the null-hypothesis of equal treatment effects on survival under the intention-to-treat principle. The latter analysis was performed as a confirmatory one, using adjusted alpha-levels according to Bonferroni-Holm[3] and was the only one upon which to base decisions about the effect of pindolol on survival.

Exploratory data analysis is gaining increased attention in the statistical and medical literature. For the concepts of exploratory/confirmatory data analysis see also [4] and [5]. The exploratory discriminant analysis was applied in the backward stepwise manner, to show variables which possibly may have a joint effect on total cardiac mortality.

This method considers the effect of any variable additional to that of those variables which are still in the model and excludes the less important one of any two highly correlated variables. Therefore, such a discriminant analysis will yield the most economic significant model' consisting of the smallest possible number of variables to classify patients as alive or dead. It was preferred to the analysis of many unconnected contingency tables (variable *v.* alive/dead), which method, exploratory also, would not have considered the correlation between the variables.

Any stepwise procedure such as the discriminant analysis performed is per se exploratory in nature since decisions about retaining or excluding variables in the model are data-dependent. Accordingly, in a confirmatory approach (aiming at *P* values to base decisions upon) stepwise procedures would have no place, and naturally, the confirmatory analysis model would have to include the main effects which generated the interactions also contained in the model.

The fact that a variable shows up as being 'significant' in an exploratory analysis means that in future studies this variable should cause special interest and further investigation.

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[5] Holm S. A simple sequentially rejective multiple test procedure. Scand J Stat 1979; 65–70.